

(Submitted via Internet November 30, 2001.)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Methanol.

The American Methanol Institute Testing Group [AMITG] concludes that no additional testing is required under the HPV testing program. We concur with this conclusion based on our review of the robust summaries as well as numerous research articles on methanol toxicity published in the open scientific literature.

Methanol exposures come from a wide variety of sources including its use as a solvent, in chemical syntheses and its presence in foodstuffs. Its toxicity in people has been reported in numerous clinical studies; the most notable effect appears to be ocular toxicity including blindness. Although very high exposures are lethal, the acute toxicity to aquatic life and humans is low. It does not appear to be carcinogenic in rodents although formaldehyde is a metabolite. Methanol is not genotoxic. Existing information from repeat dose studies is adequate to establish a NOEL in several test species for chronic exposures given the rapid metabolism and clearance of methanol. Likewise, the literature contains studies examining methanol toxicity when administered via different routes including oral, inhalation, and drinking water.

Developmental toxicity appears to be the toxic endpoint of greatest concern. Traditional teratology studies reveal a NOEL of 1000 ppm in mice for cervical ribs and vertebrae changes. Mice are more sensitive than rats to the developmental toxicity of methanol. Developmental neurobehavioral effects of methanol are currently being investigated in a number of laboratories and we recommend that EPA and AMITG keep abreast of those studies for prioritizing possible post-HPV activities.

Methanol was recently reviewed by the NTP Center for the Evaluation of Risks to Human Reproduction [CERHR]. The expert panel convened to conduct the review made several conclusions regarding dose-response relationships for methanol and the derivation of benchmark doses, NOELs and LOELs for reproductive and developmental endpoints. The panel will also make several recommendations on research needs when the report is released in the near future. While these recommendations will likely be most appropriate for post-HPV plans, AMITG and EPA should use the report to help guide research plans and health and safety assessments. These research needs include but are not limited to the following:

1. Evaluation of the normal range of blood levels for methanol and formaldehyde in the U.S. population using NHANES or other exposure initiatives.
2. Evaluation of the possibility that some individuals might be especially sensitive to the developmental toxicity of methanol based on genetic differences in methanol metabolism and other factors governing folate status.
3. Ethanol is metabolized via similar pathways as methanol, and both are developmental toxicants. Since co-exposure to both methanol and ethanol are likely to occur studies are needed

to determine if effects are additive, synergistic, or antagonistic.

Thank you for this opportunity to comment.

George Lucier, Ph.D.

Consulting Toxicologist, Environmental Defense

Karen Florini

Senior Attorney, Environmental Defense